

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claims 1-8 (Previously Cancelled)

Claim 9 (Presently Amended) A method for inhibiting synovial cell growth, comprising administering to a patient in need thereof a pharmaceutical composition comprising ~~an~~ humanized PM-1 antibody ~~including a set of complementarity determining regions of an antibody produced by FERM BP-2998 hybridoma~~ and a physiologically acceptable carrier.

Claim 10 (Presently Cancelled)

Claim 11 (Previously Added) The method according to claim 9, wherein the patient is a human.

Claim 12 (Previously Added) The method according to claim 11, wherein the antibody is administered in four divided doses from about 1 to 1000 mg.

D₁ Claim 13 (Presently Amended) A method of treating chronic rheumatoid arthritis, comprising administering to a patient in need thereof a pharmaceutical composition comprising ~~an~~ humanized PM-1 antibody ~~including a set of complementarity determining regions of an antibody produced by FERM BP-2998 hybridoma~~ and a physiologically acceptable carrier.

Claim 14 (Previously Added) The method according to claim 13, wherein the antibody suppresses abnormal growth of synovial cells.

Claim 15 (Presently Cancelled)

Claim 16 (Previously Added) The method according to claim 13, wherein the patient is a human.

Claim 17 (Previously Added) The method according to claim 16, wherein the antibody is administered in four divided doses from about 1 to 1000 mg.

Claim 18 (Presently Added) A method according to claim 9, wherein said humanized PM-1 antibody comprises

(A) L chains of an antibody to said human IL-6 receptor, each comprising:

(1) a variable (V) region of a light (L) chain of an antibody to the human IL-6 receptor having the following structure:

FR1¹-CDR1¹-FR2¹-CDR2¹-FR3¹-CDR3¹-FR4¹

wherein CDR1¹, CDR2¹ and CDR3¹ represent a set of three complementarity determining regions comprising a set of the following amino acid sequences:

CDR1¹ Arg Ala Ser Gln Asp Ile Ser Ser Tyr Leu Asn

CDR2¹ Tyr Thr Ser Arg Leu His Ser

CDR3¹ Gln Gln Gly Asn Thr Leu Pro Tyr Thr;

and the FR1¹, FR2¹, FR3¹ and FR4¹ comprise a set of the following amino acid sequences:

FR1¹ Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala
Ser Val Gly Asp Arg Val Thr Ile Thr Cys

FR2¹ Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu
Ile Tyr

FR3¹ Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr
Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp
Ile Ala Thr Tyr Tyr Cys

FR4¹ Phe Gly Gln Gly Thr Lys Val Glu Ile Lys;

or

FR1¹ Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala
Ser Val Gly Asp Arg Val Thr Ile Thr Cys

FR2¹ Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu
Ile Tyr

FR3¹ Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr
Asp Tyr Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp
Ile Ala Thr Tyr Tyr Cys

FR4¹ Phe Gly Gln Gly Thr Lys Val Glu Ile Lys;

and

(2) a C region of an L chain of a human antibody C κ ; and N

(B) H chains of an antibody to the human IL-6 receptor, each comprising:

(1) a V region of a heavy (H) chain of an antibody to the human IL-6 receptor having the following structure:

FR1²-CDR1²-FR2²-CDR2²-FR3²-CDR3²-FR4²

wherein CDR1² CDR2² and CDR3² represent a set of three complementarity determining regions comprising a set of the following amino acid sequences:

CDR1² Ser Asp His Ala Trp Ser

CDR2² Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
Lys Ser

CDR3² Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr;

and the FR1², FR2², FR3² and FR4² comprise a set of the following amino acid sequences:

FR1² Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg
Pro Ser Gln Thr Leu Ser Leu Thr Cys Thr Val Ser Gly
Tyr Ser Ile Thr

FR2² Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile
Gly

FR3² Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe
Ser Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala
Val Tyr Tyr Cys Ala Arg

FR4² Trp Gly Gln Gly Ser Leu Val Thr Val Ser Ser; and

(2) a C region of an H chain of a human antibody C γ .

Please amend the specification as follows.

Please replace the paragraph bridging pages 10-11 with the following paragraph.

--Reshaped human antibodies may also be used according to the invention. These are prepared by using the complementary determinant region of a mouse or other non-human mammalian animal antibody to replace the complementary determinant region of a human antibody, and conventional gene recombination methods therefor are well-known. One of the known methods may be used to obtain a reshaped human antibody which is useful according to the invention. A preferred example of such a reshaped human antibody is hPM-1 (see Intl. Unexamined Patent Application No. WO92-19759, which includes a humanized PM-1 antibody that comprises:

(A) L chains of an antibody to the human IL-6 receptor, each comprising:

(1) a variable (V) region of a light (L) chain of an antibody to the human IL-6 receptor having the following structure:

FR1¹-CDR1¹-FR2¹-CDR2¹-FR3¹-CDR3¹-FR4¹

wherein CDR1¹, CDR2¹ and CDR3¹ represent a set of three complementarity determining regions comprising a set of the following amino acid sequences:

CDR1¹ Arg Ala Ser Gln Asp Ile Ser Ser Tyr Leu Asn

CDR2¹ Tyr Thr Ser Arg Leu His Ser

CDR3¹ Gln Gln Gly Asn Thr Leu Pro Tyr Thr;

and the FR1¹, FR2¹, FR3¹ and FR4¹ comprise a set of the following amino acid sequences:

FR1¹ Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala
Ser Val Gly Asp Arg Val Thr Ile Thr Cys

FR2¹ Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu
Ile Tyr

FR3¹ Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr
Asp Phe Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp
Ile Ala Thr Tyr Tyr Cys

FR4¹ Phe Gly Gln Gly Thr Lys Val Glu Ile Lys;

or

FR1¹ Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala
Ser Val Gly Asp Arg Val Thr Ile Thr Cys

FR2¹ Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu
Ile Tyr

FR3¹ Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr
Asp Tyr Thr Phe Thr Ile Ser Ser Leu Gln Pro Glu Asp
Ile Ala Thr Tyr Tyr Cys

FR4¹ Phe Gly Gln Gly Thr Lys Val Glu Ile Lys;

and

(2) a C region of an L chain of a human antibody Cκ; and N

(B) H chains of an antibody to the human IL-6 receptor, each comprising:

(1) a V region of a heavy (H) chain of an antibody to the human IL-6
receptor having the following structure:

FR1²-CDR1²-FR2²-CDR2²-FR3²-CDR3²-FR4²

wherein CDR1² CDR2² and CDR3² represent a set of three
complementarity determining regions comprising a set of the following
amino acid sequences:

CDR1² Ser Asp His Ala Trp Ser

CDR2² Tyr Ile Ser Tyr Ser Gly Ile Thr Thr Tyr Asn Pro Ser Leu
Lys Ser

CDR3² Ser Leu Ala Arg Thr Thr Ala Met Asp Tyr;

and the FR1², FR2², FR3² and FR4² comprise a set of the following
amino acid sequences:

FR1² Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Arg
Pro Ser Gln Thr Leu Ser Leu Thr Cys Thr Val Ser Gly
Tyr Ser Ile Thr

FR2² Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile
Gly

FR3² Arg Val Thr Met Leu Arg Asp Thr Ser Lys Asn Gln Phe
Ser Leu Arg Leu Ser Ser Val Thr Ala Ala Asp Thr Ala
Val Tyr Tyr Cys Ala Arg

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FR4² Trp Gly Gln Gly Ser Leu Val Thr Val Ser Ser; and
(2) a C region of an H chain of a human antibody C_γ).--
